Placental growth factor expression is required for bone marrow endothelial cell support of primitive murine hematopoietic cells.

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Public Summary:
Our data demonstrate that endothelial cells in the bone marrow vascular niche are involved in the regeneration of hematopoietic stem/progenitor cells and that placenta growth factor plays a role in this overall process.

Scientific Abstract:
Two distinct microenvironmental niches that regulate hematopoietic stem/progenitor cell physiology in the adult bone marrow have been proposed; the endosteal and the vascular niche. While extensive studies have been performed relating to molecular interactions in the endosteal niche, the mechanisms that regulate hematopoietic stem/progenitor cell interaction with bone marrow endothelial cells are less well defined. Here we demonstrate that endothelial cells derived from the bone marrow supported hematopoietic stem/progenitor cells to a higher degree than other endothelial or stromal cell populations. This support was dependant upon placental growth factor expression, as genetic knockdown of mRNA levels reduced the ability of endothelial cells to support hematopoietic stem/progenitor cells in vitro. Furthermore, using an in vivo model of recovery from radiation induced myelosuppression, we demonstrate that bone marrow endothelial cells were able to augment the recovery of the hematopoietic stem/progenitor cells. However, this effect was diminished when the same cells with reduced placental growth factor expression were administered, possibly owing to a reduced homing of the cells to the bone marrow vasculature. Our data suggest that placental growth factor elaborated from bone marrow endothelial cells mediates the regulatory effects of the vascular niche on hematopoietic stem/progenitor cell physiology.